Nondestructive fluorescence lifetime imaging and time-resolved fluorescence spectroscopy detect cartilage matrix depletion and correlate with mechanical properties.

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Public Summary:
Tissue engineering holds great promise for the functional replacement of damaged and diseased articular cartilage. Translating these tissue engineered solutions into clinical practice and commercialization faces several current challenges including the need for continuous evaluation of tissue maturation to ensure the desired biochemical and mechanical properties are achieved for successful implantation. Currently, tissue engineers rely on destructive and time-consuming techniques that require complete or partial sample loss. A nondestructive solution to monitor tissue maturation would reduce costs and accelerate product development. As a first step toward this goal, two nondestructive, label-free optical techniques based on tissue autofluorescence, namely multispectral fluorescent lifetime imaging (FLIm) and time-resolved fluorescence spectroscopy (TRFS), were investigated for their potential in evaluating the biochemical and mechanical properties of articular cartilage. Articular cartilage samples were treated with enzymes to mimic the early stages of osteoarthritis by selectively decreasing the two major structural components of cartilage (collagen and proteoglycan). Samples were assessed for their optical properties using a fiber-coupled optical system combining FLIm and TRFS, their biochemical and mechanical properties, and by histological staining. The optical measurements were sensitive to changes in cartilage matrix and correlated with mechanical and biochemical assays. Optical data from fluorescence lifetime values extracted from FLIm images (375-410 nm spectral band) showed strong, specific correlations with collagen content and tensile strength while fluorescence lifetime values centered at 520 nm (with a 5 nm bandwidth) possessed strong, specific correlations with proteoglycan content and compressive properties. The hypothesis that noninvasive assessments could be used to infer the changes in both the biochemical composition and biomechanical properties of cartilage that occur during matrix depletion was supported by the strong linear correlations between destructive and nondestructive tests, making this the first investigation that demonstrated quantitative relationships between fluorescence LT and articular cartilage mechanical properties. The development of nondestructive tools with the potential to monitor the functional properties of tissue engineered articular cartilage holds great potential for research, industrial, and clinical applications.

Scientific Abstract:
Tissue engineers utilize a battery of expensive, time-consuming and destructive techniques to assess the composition and function of engineered tissues. A nondestructive solution to monitor tissue maturation would reduce costs and accelerate product development. As a first step toward this goal, two nondestructive, label-free optical techniques, namely multispectral fluorescent lifetime imaging (FLIm) and time-resolved fluorescence spectroscopy (TRFS), were investigated for their potential in evaluating the biochemical and mechanical properties of articular cartilage. Enzymatic treatments were utilized to selectively deplete cartilage of either collagen or proteoglycan, to produce a range of matrix compositions. Samples were assessed for their optical properties using a fiber-coupled optical system combining FLIm and TRFS, their biochemical and mechanical properties and by histological staining. Single and multivariable correlations were performed to evaluate relationships among these properties. FLIm- and TRFS-derived measurements are sensitive to changes in cartilage matrix and correlate with mechanical and biochemical assays. Mean fluorescence lifetime values extracted from FLIm images (375-410 nm spectral band) showed strong, specific correlations with collagen content ($R2 = 0.79$, $p < 0.001$) and tensile properties ($R2 = 0.45$, $p = 0.02$). TRFS lifetime measurements centered at 520 nm (with a 5 nm bandwidth) possessed strong, specific correlations with proteoglycan content ($R2 = 0.59$, $p = 0.001$) and compressive properties ($R2 = 0.71$, $p < 0.001$). Nondestructive optical assessment of articular cartilage, using a combination of FLIm- and TRFS-derived parameters, provided a quantitative method for determining tissue biochemical composition and mechanical function. These tools hold great potential for research, industrial and clinical settings.

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